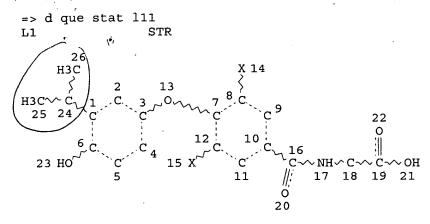
## Scientific and Technical Information Center

## SEARCH REQUEST FORM

Requester's Full Name: S. Kuwar Examiner #: 69594 Date: 875 Art Unit: 1621 Phone Number: 2-0640 Serial Number: 10580 902
Art Unit: 161 Phone Number: 2-0640 Serial Number: 10/580 902  Location (Bldg/Room#): R-W (Mailbox #): 508 Results Format Preferred (circle) PAPER  ***********************************
To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:
Title of Invention: Novel Confounds
Inventors (please provide full names): Neeray Garg et al.
Earliest Priority Date: 7/10/02
<ol> <li>(Original) N-[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)benzoyl] glycine (E1);</li> </ol>
N-[3,5-Dichloro-4-(3-bromo-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E2);
N-[3,5-Dichloro-4-(2-bromo-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E3);
N-[3,5-Dichloro-4-(3-chloro-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E4);
N-[3,5-Dichloro-4-(3-cyano-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E5);
N-[3,5-Dichloro-4-(3-fluoro-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E6)
N-[3,5-Dichloro-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E7)
L-N-[3,5-Dibromo-4-(3-fluoro-4-hydroxy-5-isopropylphenoxy)phenylacetyl] valine (E10)
D-N-[3,5-Dibromo-4-(3-chloro-4-hydroxy-5- isopropylphenoxy)phenylacetyl] phenylglycine (E11)
L-N-[3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)phenylacetyl] valine (E12)
L-N-[3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)phenylacetyl]phenylglycine (E13)
L-N-{3,5-Dibromo-4-(3,5-dimethyl-4-hydroxyphenoxy)phenylacetyl}-phenylglycine (E14)
N-[3,5-Dibromo-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E8)
N-[3,5-Dimethyl-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (E9).
2. (Canceled)

- 3. (Original) A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a pharmaceutically effective salt thereof, together with a pharmaceutically acceptable carrier.
- 4. (Original) A process for making a pharmaceutical composition comprising combining a compound according to

HIS PAGE LEFT BLANK



NODE ATTRIBUTES:

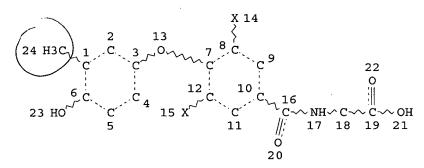
DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

**GRAPH ATTRIBUTES:** 

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE

L3. 44 SEA FILE=REGISTRY SSS FUL L1
L4 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE

L6 3 SEA FILE=REGISTRY SSS FUL L4

L7 44 SEA FILE=REGISTRY ABB=ON L3 OR L6

L8 3 SEA FILE=HCAPLUS ABB=ON L7

L9 2 SEA FILE=HCAPLUS ABB=ON L8 AND (PRD<20020710 OR PD<20020710)
L10 3 SEA FILE=USPATFULL ABB=ON L8 AND (PRD<20020710 OR PD<20020710)

L11 5 DUP REMOV L9 L10 (0 DUPLICATES REMOVED)

=> d ibib abs hitstr ll1 1-5

L11 ANSWER 1 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2006:17927 USPATFULL

TITLE:

INVENTOR(S):

Thyroid receptor ligands and method II

Hangeland, Jon, Morrisville, PA, UNITED STATES

Zhang, Minsheng, Warren, NJ, UNITED STATES

Caringal, Yolanda, Lawrenceville, NJ, UNITED STATES

Ryono, Denis, Princeton, NJ, UNITED STATES

Li, Yi-Lin, Huddinge, SWEDEN Malm, Johan, Skogas, SWEDEN Liu, Ye, Tullinge, SWEDEN Garg, Neeraj, Tumba, SWEDEN Litten, Chris, Tumba, SWEDEN

Collazo, Ana Maria Garcia, Stockholm, SWEDEN

Koehler, Konrad, Huddinge, SWEDEN

PATENT ASSIGNEE(S): Karo Bio AB, Huddinge, SWEDEN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6989402	B1	20060124	
THIENT INTOICEMENT	WO 2000039077	21	20000706	<
APPLICATION INFO.:	US 2001-868889		19991223	(9)
	WO 1999-IB2084		19991223	D.C
			20010914	PCT 371 date

NUMBER DATE

PRIORITY INFORMATION:

GB 1998-28442 19981224 <--

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: McKane, Joseph K. ASSISTANT EXAMINER: Coppins, Janet L.

ASSISTANT EXAMINER: Coppins, Janet L.

LEGAL REPRESENTATIVE: Garabedian, Todd E., Wiggin and Dana LLP

NUMBER OF CLAIMS: 21 EXEMPLARY CLAIM: 1

EXEMPLARY CLAIM: 1 LINE COUNT: 1966

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

New thyroid receptor ligands are provided which have general formula (I) in which: n is an integer from 0 to 4; R.sub.1 is halogen, trifluoromethyl, or alkyl of 1 to 6 carbons or cycloalkyl of 3 to 7 carbons; R.sub.2 and R.sub.3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, at least one of R.sub.2 and R.sub.3 being other than hydrogen; R.sub.4 is a carboxylic acid amide (CONR'R") or an acylsulphonamide (CONHSO2R') derivative, or a pharmaceutically acceptable salt thereof, and all stereoisomers thereof; or when n is equal to or greater than one, R.sub.4 may be a heteroaromatic moiety which may be substituted or unsubstituted, or an amine (NR'R"). R.sub.5 is hydrogen or an acyl (such as acetyl or benzoyl) or other group capable of bioconversion to generate the free phenol structure (wherein R.sub.5=H). In addition, a method is provided for preventing, inhibiting or treating a disease associated with metabolism dysfunction or which is dependent upon the expression of a T.sub.3 regulated gene, wherein a compound as described above is administered in a therapeutically effective amount. Examples of such diseases associated with metabolism dysfunction or are dependent upon the expression of a T.sub.3 regulated gene include obesity, hypercholesterolemia, atherosclerosis, cardiac arrhythmias, depression, osteoporosis, hypothyroidism, goiter, thyroid cancer as well as glaucoma, congestive heart failure and skin disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 280777-33-5P 280777-34-6P 280777-35-7P 280777-36-8P 280777-37-9P 280777-38-0P

280777-39-1P 280777-40-4P 280777-42-6P .280777-43-7P 280777-44-8P 280777-45-9P 280777-46-0P 280777-47-1P 280777-48-2P 280777-50-6P 280777-51-7P 280777-52-8P 280777-53-9P 280777-54-0P 280777-55-1P 280777-56-2P 280777-57-3P 280777-58-4P 280777-88-0P 280779-25-1P 280779-31-9P 280779-32-0P

(preparation of (hydroxyphenoxy)phenylacetyl amino acids and related compds. as novel thyroid receptor ligands)

RN 280777-33-5 USPATFULL

CN

D-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$i-Pr$$
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 
 $OH$ 

RN 280777-34-6 USPATFULL

CN D-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$i-Bu$$
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 
 $OH$ 

RN 280777-35-7 USPATFULL

CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-S-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 280777-36-8 USPATFULL

CN D-Tyrosine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-37-9 USPATFULL

CN L-Ornithine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 280777-38-0 USPATFULL

CN Butanoic acid, 2-[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

RN 280777-39-1 USPATFULL

CN L-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-40-4 USPATFULL

CN L-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-42-6 USPATFULL

CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$R$$
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 

RN 280777-43-7 USPATFULL

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 280777-44-8 USPATFULL

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$ 
 $S$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 

RN 280777-45-9 USPATFULL

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$_{\text{H}_{2}\text{N}}$$
 (CH<sub>2</sub>)<sub>4</sub>  $_{\text{R}}$   $_{\text{N}}$   $_{\text{CO}_{2}\text{H}}$   $_{\text{O}}$   $_{\text{i-Pr}}$   $_{\text{oh}}$ 

RN 280777-46-0 USPATFULL

CN Alanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-2-methyl- (9CI) (CA INDEX NAME)

RN 280777-47-1 USPATFULL

CN Benzeneacetic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-48-2 USPATFULL

CN Benzeneacetic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-,  $(\alpha R)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$Br$$
 $O$ 
 $Br$ 
 $OH$ 
 $OH$ 
 $OH$ 

RN 280777-50-6 USPATFULL

CN Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-α-methyl- (9CI) (CA INDEX NAME)

RN 280777-51-7 USPATFULL

CN L-Isoleucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-52-8 USPATFULL

CN D-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-53-9 USPATFULL

CN L-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1 methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

RN 280777-54-0 USPATFULL

CN L-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-55-1 USPATFULL

CN D-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-56-2 USPATFULL

CN Cyclohexanepropanoic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

RN 280777-57-3 USPATFULL

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-58-4 USPATFULL

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-88-0 USPATFULL

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 280779-25-1 USPATFULL

CN D-Methionine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

MeS 
$$R$$
  $N$   $C1$   $OH$   $CO_2H$   $O$   $i-Pr$ 

RN 280779-31-9 USPATFULL

CN L-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

HO S N C1 OH 
$$C1$$
 OH

RN 280779-32-0 USPATFULL

CN D-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

HO R N C1 OH 
$$C1$$
 OH  $i-Pr$ 

L11 ANSWER 2 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2005:324960 USPATFULL

TITLE: Novel thyroid receptor ligands and method II
INVENTOR(S): Hangeland, Jon, Morrisville, PA, UNITED STATES

Zhang, Minsheng, Warren, NJ, UNITED STATES

Caringal, Yolanda, Lawrenceville, NJ, UNITED STATES

Ryono, Denis, Princeton, NJ, UNITED STATES

Li, Yi-Lin, Huddinge, SWEDEN
Malm, Johan, Skogas, SWEDEN
Liu, Ye, Tullinge, SWEDEN
Garg, Neeraj, Tumba, SWEDEN
Litten, Chris, Tumba, SWEDEN

Collazo, Ana Maria Garcia, Stockholm, SWEDEN

Koehler, Konrad, Huddinge, SWEDEN

	NUMBER	KIND	DATE
US	2005282872	A1	20051222

PATENT INFORMATION: APPLICATION INFO.:

US 2005282872 AT 20051222 US 2005-189654 AT 20050726 (11)

RELATED APPLN. INFO.:

Division of Ser. No. US 2001-868889, filed on 14 Sep 2001, PENDING A 371 of International Ser. No. WO

1999-IB2084, filed on 23 Dec 1999

NUMBER	DATE						
	10001001						

PRIORITY INFORMATION:

GB 1998-28442

19981224

DOCUMENT TYPE: FILE SEGMENT: Utility APPLICATION

LEGAL REPRESENTATIVE:

WIGGIN AND DANA LLP, ATTENTION: PATENT DOCKETING, ONE

CENTURY TOWER, P.O. BOX 1832, NEW HAVEN, CT,

06508-1832, US

NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 2022

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

New thyroid receptor ligands are provided which have general formula (I) in which: n is an integer from 0 to 4; R.sub.1 is halogen, trifluoromethyl, or alkyl of 1 to 6 carbons or cycloalkyl of 3 to 7 carbons; R.sub.2 and R.sub.3 are the same or differential hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, at least one of R.sub.2 and R.sub.3 being other than hydrogen; R.sub.4 is a carboxylic acid thereof; or when n is equal to or greater than one, R.sub.4 may be heteroaromatic moiety which may be substituted or unsubstituted, or an amine (NR'R"). R.sub.5 is hydrogen or an acyl (such as acetyl or benzoyl) or other group capable of bioconversion to generate the free phenol structure (wherein R.sub.5--H). In addition, a method is provided for preventing, inhibiting or treating a disease

associated with metabolism dysfunction or which is dependant upon the expression of a T.sub.3 regulated gene, wherein a compound as described above is administered in a therapeutically effective amount. Examples of such diseases associated with metabolism dysfunction or are dependent upon the expression of a T.sub.3 regulated gene include obesity, hypercholesterolemia, atherosclerosis, cardiac arrhythmias, depression, osteoporosis, hypothyroidism, goiter, thyroid cancer as well as glaucoma, congestive heart failure and skin disorders. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 280777-33-5P 280777-34-6P 280777-35-7P 280777-36-8P 280777-37-9P 280777-38-0P 280777-39-1P 280777-40-4P 280777-42-6P 280777-43-7P 280777-44-8P 280777-45-9P 280777-46-0P 280777-47-1P 280777-48-2P 280777-50-6P 280777-51-7P 280777-52-8P 280777-53-9P 280777-54-0P 280777-55-1P 280777-56-2P 280777-57-3P 280777-58-4P 280777-88-0P 280779-25-1P 280779-31-9P 280779-32-0P (preparation of (hydroxyphenoxy)phenylacetyl amino acids and related compds. as novel thyroid receptor ligands) RN280777-33-5 USPATFULL D-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-CN (CA INDEX NAME)

Absolute stereochemistry.

$$i-Pr$$
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 
 $OH$ 

RN 280777-34-6 USPATFULL CN D-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$i-Bu$$
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 
 $OH$ 

RN 280777-35-7 USPATFULL CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-S-(phenylmethyl)- (9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 280777-36-8 USPATFULL

CN D-Tyrosine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-37-9 USPATFULL

CN L-Ornithine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 280777-38-0 USPATFULL

CN Butanoic acid, 2-[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-39-1 USPATFULL

CN L-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-40-4 USPATFULL

CN L-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$i-Bu$$
  $S$   $N$   $Br$   $OH$   $i-Pr$ 

RN 280777-42-6 USPATFULL

CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\text{HS}}$$
 $_{\text{CO}_{2}\text{H}}$ 
 $_{\text{O}}$ 
 $_{\text{i-Pr}}$ 
 $_{\text{OH}}$ 

RN 280777-43-7 USPATFULL

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$Br$$
 $O$ 
 $Br$ 
 $O$ 
 $i-Pr$ 
 $O$ 

RN 280777-44-8 USPATFULL

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$H_2N$$
 $(CH_2)_4$ 
 $S$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 

RN 280777-45-9 USPATFULL

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\text{H}_2\text{N}}$$
  $_{\text{CO}_2\text{H}}^{\text{CO}_2\text{H}}$   $_{\text{O}}^{\text{Br}}$   $_{\text{i-Pr}}^{\text{OH}}$ 

RN 280777-46-0 USPATFULL

CN Alanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-2-methyl- (9CI) (CA INDEX NAME)

RN 280777-47-1 USPATFULL

CN Benzeneacetic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$Br$$
 $O$ 
 $Br$ 
 $OH$ 
 $OH$ 
 $OH$ 

RN 280777-48-2 USPATFULL

CN Benzeneacetic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Ext. 22524

100

RN 280777-50-6 USPATFULL

CN Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-α-methyl- (9CI) (CA INDEX NAME)

RN 280777-51-7 USPATFULL

CN L-Isoleucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-52-8 USPATFULL

CN D-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

RN 280777-53-9 USPATFULL

CN L-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

MeS 
$$S$$
  $N$   $Br$   $OH$   $i-Pr$ 

RN 280777-54-0 USPATFULL

CN L-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-55-1 USPATFULL

CN D-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-56-2 USPATFULL

CN Cyclohexanepropanoic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

sum .

RN 280777-57-3 USPATFULL

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-58-4 USPATFULL

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$Ph$$
 $O$ 
 $M$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 

RN 280777-88-0 USPATFULL

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 280779-25-1 USPATFULL
CN D-Methionine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

MeS 
$$R$$
  $N$   $C1$   $OH$   $CO_2H$   $O$   $i-Pr$ 

RN 280779-31-9 USPATFULL

CN L-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

HO S N C1 OH 
$$C1$$
 OH  $i-Pr$ 

RN 280779-32-0 USPATFULL

CN D-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

HO 
$$\stackrel{\text{R}}{\longrightarrow}$$
  $\stackrel{\text{N}}{\longrightarrow}$   $\stackrel{\text{Cl}}{\longrightarrow}$   $\stackrel{\text{OH}}{\longrightarrow}$   $\stackrel{\text{Cl}}{\longrightarrow}$   $\stackrel{\text{OH}}{\longrightarrow}$ 

L11 ANSWER 3 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2002:122675 USPATFULL

TITLE: Benzamide ligands for the thyroid receptor INVENTOR(S): Ryono, Denis E., Princeton, NJ, United States

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, Princeton, NJ, United

States (U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION: US 2000-210102P 20000607 (60) <--

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Killos, Paul J. LEGAL REPRESENTATIVE: Kilcoyne, John M.

NUMBER OF CLAIMS: 29 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT: 982

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB New thyroid receptor ligands are provided which have the general formula ##STR1##

in which:

X is --O--, --S--, --CH.sub.2--, --CO--, or --NH--;

R.sub.1 is halogen, trifluoromethyl, or alkyl of 1 to 6 carbons or cycloalkyl of 3 to 7 carbons;

R.sub.2 and R.sub.3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons, at least one of R.sub.2 and R.sub.3 being other than hydrogen;

R.sub.4 is methyl, ethyl, n-propyl or trifluoromethyl;

R.sub.5 is hydrogen or lower alkyl;

R.sub.6 is carboxylic acid, or esters or prodrugs;

R.sub.7 is hydrogen or an alkanoyl or an aroyl.

In addition, a method is provided for preventing, inhibiting or treating

a disease associated with metabolism dysfunction or which is dependent upon the expression of a T.sub.3 regulated gene, wherein a compound as described above is administered in a therapeutically effective amount. Examples of such diseases associated with metabolism dysfunction or are dependent upon the expression of a T.sub.3 regulated gene include obesity, hypercholesterolemia, atherosclerosis, cardiac arrhythmias, depression, osteoporosis, hypothyroidism, goiter, thyroid cancer as well as glaucoma, congestive heart failure and skin disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 280777-88-0P 378786-34-6P 378786-35-7P

378786-36-8P 378786-37-9P 378786-38-0P

378786-39-1P 378786-40-4P 378786-41-5P

((aryloxy)benzamide ligands for thyroid receptor)

RN 280777-88-0 USPATFULL

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 378786-34-6 USPATFULL

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-methylbenzoyl]- (9CI) (CA INDEX NAME)

RN 378786-35-7 USPATFULL

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)

RN 378786-36-8 USPATFULL

CN Glycine, N-[3,5-dibromo-2-ethyl-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & \text{Et} & & & \\ & & \text{O} & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 378786-37-9 USPATFULL

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-propylbenzoyl]- (9CI) (CA INDEX NAME)

RN 378786-38-0 USPATFULL

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-methylbenzoyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & \text{Me} & & & \\ & \text{HO}_2\text{C-CH}_2\text{-NH-C} & & & \\ & & & & \\ & \text{O} & & & \\ & & & & \\ \end{array}$$

RN 378786-39-1 USPATFULL

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)

RN 378786-40-4 USPATFULL

Glycine, N-[3,5-dichloro-2-ethyl-4-[4-hydroxy-3-(1-CN methylethyl)phenoxy]benzoyl] - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Cl} \\ & \text{Et} \\ & \text{O} \\ & \text{HO}_2\text{C}-\text{CH}_2-\text{NH}-\text{C} \\ & \text{O} \\ & \text{O} \\ & \text{O} \\ & \text{O} \\ \end{array}$$

378786-41-5 USPATFULL RN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-CN propylbenzoyl] - (9CI) (CA INDEX NAME)

L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:904080 HCAPLUS

DOCUMENT NUMBER:

136:19947

TITLE:

Benzamide ligands for the thyroid receptor

INVENTOR(S):

Ryono, Denis E.

PATENT ASSIGNEE(S):

Bristol-Myers Squibb Company, USA

SOURCE:

PCT Int. Appl., 38 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE				
	A2		WO 2001-US17742	20010601 <				
WO 2001094293	A3	20020606						
W: AE, AG,	L, AM, AT,	, AU, AZ, BA	A, BB, BG, BR, BY,	BZ, CA, CH, CN,				
CR, CU,	Z, DE, DK,	, DM, DZ, EE	E, ES, FI, GB, GD,	GE, GH, GM, HR,				
HU, ID,	L, IN, IS,	, JP, KE, KC	G, KP, KR, KZ, LC,	LK, LR, LS, LT,				
LU, LV, I	A, MD, MG,	, MK, MN, MV	W, MX, MZ, NO, NZ,	PL, PT, RO, RU,				
SD, SE,	G, SI, SK,	, SL, TJ, TN	M, TR, TT, TZ, UA,	UG, US, UZ, VN,				
YU, ZA,	W, AM, AZ,	, BY, KG, K2	Z, MD, RU, TJ, TM					
RW: GH, GM,	E, LS, MW,	, MZ, SD, SI	L, SZ, TZ, UG, ZW,	AT, BE, CH, CY,				
DE, DK,	S, FI, FR,	, GB, GR, IE	E, IT, LU, MC, NL,	PT, SE, TR, BF,				
BJ, CF,	G, CI, CM,	, GA, GN, GV	W, ML, MR, NE, SN,	TD, TG				
US 6395784	B1	B1 20020528 US 2001-871347 2001053						
CA 2411062	AA	20011213	20011213 CA 2001-2411062 200106					
AU 2001068132	A5	20011217	11217 AU 2001-68132 20010601					
EP 1292568	A2	20030319	EP 2001-946036	20010601 <				

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

The second of

JP 2004524261 T2 20040812 JP 2002-501810 20010601 <--

PRIORITY APPLN. INFO.: US 2000-210102P P 20000607 <-- WO 2001-US17742 W 20010601 <--

Ι

OTHER SOURCE(S): MARPAT 136:19947

GI

AB Benzamides such as I were prepared for preventing, inhibiting or treating a disease associated with metabolism dysfunction or which is dependent upon the expression of a T3 regulated gene. Thus, I was prepared in 5 steps starting from 4'-hydroxy-2'-methylacetophenone and proceeding via II (R = Me, H).

IT 280777-88-0P 378786-34-6P 378786-35-7P 378786-36-8P 378786-37-9P 378786-38-0P 378786-39-1P 378786-40-4P 378786-41-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

((aryloxy)benzamide ligands for thyroid receptor)

RN 280777-88-0 HCAPLUS

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 378786-34-6 HCAPLUS

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2methylbenzoyl]- (9CI) (CA INDEX NAME)

RN 378786-35-7 HCAPLUS

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)

RN 378786-36-8 HCAPLUS

CN Glycine, N-[3,5-dibromo-2-ethyl-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HO}_2\text{C}-\text{CH}_2-\text{NH}-\text{C} & & & \\ & & & \\ \text{O} & & & \\ \text{i-Pr} & & \\ \end{array}$$

RN 378786-37-9 HCAPLUS

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-propylbenzoyl]- (9CI) (CA INDEX NAME)

$$Br$$
 $OHO_2C-CH_2-NH-C$ 
 $OHO_2C$ 

RN 378786-38-0 HCAPLUS

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-methylbenzoyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & \text{Me} & & & \\ & & \text{O} & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 378786-39-1 HCAPLUS

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)

RN 378786-40-4 HCAPLUS

CN Glycine, N-[3,5-dichloro-2-ethyl-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

RN 378786-41-5 HCAPLUS

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]-2-propylbenzoyl]- (9CI) (CA INDEX NAME)

L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:457018 HCAPLUS

DOCUMENT NUMBER: 133:89793

TITLE: Preparation of 4-(4-hydroxyphenoxy)phenylacetyl amino

acids and related compounds as novel thyroid receptor

ligands

INVENTOR(S): Hangeland, Jon; Zhang, Minsheng; Caringal, Yolanda;

Ryono, Denis; Li, Yi-lin; Malm, Johan; Liu, Ye; Garg, Neeraj; Litten, Chris; Garcia Collazo, Ana Maria;

Koehler, Konrad

PATENT ASSIGNEE(S):

Karo Bio AB, Swed.; et al.

SOURCE:

PCT Int. Appl., 60 pp. CODEN: PIXXD2

DOCUMENT TYPE: P

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

									APPLICATION NO.									
WO	20000	3907	7						WO 1999-IB2084									
WO	20000	3907	7		A3		2000	0921										
	W:	AE,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,	,
	(	CZ, 1	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	
		IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	
	1	MD, I	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	
		SK, S	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VN,	YU,	ZA,	zw		
	RW:	GH, (	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	ΑT,	ΒE,	CH,	CY,	DE,	
	]	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	ΝL,	PT,	SE,	BF,	ВJ,	CF,	
											SN,							
CA	23563	19			AA		2000	0706	(	CA 1	999-	2356	319		1	9991	223	<
BR	99168	51			Α		2001	1016	I	3R 1	999~	1685	1		1	9991	223	<
EP	11443	70			A2		2001	1017	]	ΞP 1	999-	9624	86		1	9991	223	<
	R: 2	AT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	FΙ															
TR	20010	1834			T2		2001	1221	5	rr 2	001-	2001	01834	4	1	9991	223	<
JP	20025	3343	2		T2		2002	1008	į.	JP 2	000-	5909	90		1	9991	223	<
AU	75820	2			B2		2003	0320	7	AU 2	000-	1885	5		1	9991	223	<
NZ	51242	2			Α		2004	0227	1	NZ 1	999-	5124	22		1	9991	223	<
NO	20010	0293	1		Α		2001	0821	1	NO 2	001-	2931			2	0010	613	<
ZA	20010	0493	2		Α		2003	0115	2	ZA 2	001-	4932			2	0010	615	<
US	69894	02			В1		2006	0124	τ	JS 2	001-	8688	89		2	0010	914	<
US	20052	8287	2		A1		2005	1222	τ	JS 2	005-	1896	54		2	0050	726	<
PRIORIT									(	3B 1	998-	2844	2 .		A 1	9981	224	<
									1	<b>VO</b> 1	999-	IB20	84	1	W 1	9991	223	<
									Ţ	JS 2	001-	8688	89		A3 2	0010	914	<
	_																	

OTHER SOURCE(S):

MARPAT 133:89793

(CH<sub>2</sub>)<sub>n</sub>-R<sup>4</sup>

 $R^{1}$ 

R3

AB Title compds. I [R1 = halo, trifluoromethyl, alkyl, cycloalkyl; R2, R3 = H, halo, alkyl, at least one of R2 and R3 being other than H; n = 0-4; R4 is an (un)substituted heteroarom. moiety linked to (CH2)n via a nitrogen or carbon atom; an amine, including those in which the amine is derived from an alpha amino acid of either L- or D-stereochem., an

acylsulfonamide, or a carboxylic acid amide, with the proviso that when n = 0, then R4 can only be a carboxylic acid amide or an acylsulfonamide; R5 is H or an acyl or other group capable of bioconversion to generate the free phenol structure] were prepared for use in the treatment of diseases associated with metabolism dysfunction or which are dependent on the expression of a T3 regulated gene (such as obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, goiter, thyroid cancer, glaucoma, cardiac arrhythmia, and congestive heart failure). Thus, coupling of 3,5-dibromo-4-(4-hydroxy-3-isopropylphenoxy)phenylacetic acid with D-methionine Me ester hydrochloride followed by hydrolysis afforded N-[3,5-dibromo-4-(4-hydroxy-3-isopropylphenoxy)phenylacetyl]-D-methionine.

IT 280777-33-5P 280777-34-6P 280777-35-7P 280777-36-8P 280777-37-9P 280777-38-0P 280777-39-1P 280777-40-4P 280777-42-6P 280777-43-7P 280777-44-8P 280777-45-9P 280777-46-0P 280777-47-1P 280777-48-2P 280777-50-6P 280777-51-7P 280777-52-8P 280777-53-9P 280777-54-0P 280777-55-1P 280777-56-2P 280777-57-3P 280777-58-4P 280777-88-0P 280779-25-1P 280779-31-9P 280779-32-0P

1005

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (hydroxyphenoxy)phenylacetyl amino acids and related compds. as novel thyroid receptor ligands)

RN 280777-33-5 HCAPLUS

CN D-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-34-6 HCAPLUS

CN D-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 280777-35-7 HCAPLUS

CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-S-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\mathrm{Ph}}$$
  $_{\mathrm{S}}$   $_{\mathrm{CO}_{2}\mathrm{H}}$   $_{\mathrm{O}}$   $_{\mathrm{i-Pr}}$   $_{\mathrm{OH}}$ 

RN 280777-36-8 HCAPLUS

CN D-Tyrosine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-37-9 HCAPLUS

CN L-Ornithine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

HO Br 
$$CO_2H$$
  $H$   $H$   $N$   $S$   $CH_2)$   $S$   $NH$   $O$   $O$ 

PAGE 1-B

J. 24.

RN 280777-38-0 HCAPLUS

CN Butanoic acid, 2-[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-39-1 HCAPLUS

CN L-Valine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$i-Pr$$
  $S$   $N$   $Br$   $OH$   $i-Pr$ 

RN 280777-40-4 HCAPLUS

CN L-Leucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$i-Bu$$
  $S$   $N$   $Br$   $OH$   $i-Pr$ 

RN 280777-42-6 HCAPLUS

CN L-Cysteine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\mathrm{HS}}$$
 $_{\mathrm{CO}_{2}\mathrm{H}}$ 
 $_{\mathrm{O}}$ 
 $_{\mathrm{i-Pr}}$ 
 $_{\mathrm{i-Pr}}$ 

RN 280777-43-7 HCAPLUS

CN Glycine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$Br$$
 $O$ 
 $Br$ 
 $O$ 
 $i-Pr$ 

RN 280777-44-8 HCAPLUS

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

$$^{\text{CH}_2\text{N}}$$
  $^{\text{CH}_2)}$   $^{\text{CH}_2}$   $^{\text{H}}$   $^{\text{OH}}$   $^{\text{OH}}$   $^{\text{OH}}$ 

RN 280777-45-9 HCAPLUS

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$ 
 $R$ 
 $N$ 
 $CO_2H$ 
 $O$ 
 $i-Pr$ 

RN 280777-46-0 HCAPLUS

CN Alanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-2-methyl- (9CI) (CA INDEX NAME)

RN 280777-47-1 HCAPLUS

CN Benzeneacetic acid, α-[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-48-2 HCAPLUS

CN Benzeneacetic acid, α-[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, (αR)- (9CI) (CA INDEX NAME)

RN 280777-50-6 HCAPLUS

CN Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-α-methyl- (9CI) (CA INDEX NAME)

RN 280777-51-7 HCAPLUS

CN L-Isoleucine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-52-8 HCAPLUS

CN D-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

MeS 
$$\stackrel{H}{\underset{CO_2H}{\text{H}}}$$
  $\stackrel{Br}{\underset{\text{i-Pr}}{\text{OH}}}$ 

RN 280777-53-9 HCAPLUS

CN L-Methionine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

MeS 
$$\stackrel{H}{\underset{CO_2H}{\bigvee}}$$
  $\stackrel{Br}{\underset{i-Pr}{\bigvee}}$   $\stackrel{O}{\underset{i-Pr}{\bigvee}}$ 

RN 280777-54-0 HCAPLUS

CN L-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-55-1 HCAPLUS

CN D-Phenylalanine, N-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-56-2 HCAPLUS

CN Cyclohexanepropanoic acid,  $\alpha$ -[[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

RN 280777-57-3 HCAPLUS

CN L-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280777-58-4 HCAPLUS

CN D-Lysine, N2-[3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$Ph$$
  $O$   $M$   $CO_2H$   $O$   $i-Pr$ 

RN 280777-88-0 HCAPLUS

CN Glycine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

RN 280779-25-1 HCAPLUS

CN D-Methionine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 280779-31-9 HCAPLUS

CN L-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

HO S N C1 OH 
$$C1$$
 OH  $i-Pr$ 

RN 280779-32-0 HCAPLUS

CN D-Serine, N-[3,5-dichloro-4-[4-hydroxy-3-(1-methylethyl)phenoxy]benzoyl](9CI) (CA INDEX NAME)

THIS PAST LET BLANT

=> d his ful

, , Y

(FILE 'HOME' ENTERED AT 14:12:53 ON 07 SEP 2006)

A STATE OF THE STATE OF

FILE 'REGISTRY' ENTERED AT 14:13:00 ON 07 SEP 2006 STR L144 SEA SSS FUL L1 with iso-Pr-seedque Stat

STR L1

0 SEA SSS SAM L4
3 SEA SSS FUL L4 with the see dque Stat

44 SEA ABB=ON L3 OR L6 L2 1.3 L4L5 L6 **L7** 

FILE 'HCAPLUS' ENTERED AT 14:17:42 ON 07 SEP 2006

L8 L9

2 SEA ABB=ON L8 AND (PRD<20020710 OR PD<20020710) Z City from CAPPLUE PATFULL' ENTERED AT 14:18:31 ON 07 SEP 2006
3 SEA ABB=ON L8 AND (PRD<20020710 OR PD<20020710) 3 City from US Batfull
APLUS, USPATFULL' ENTERED AT 14:18:43 ON 07 SEP 2006 FILE 'USPATFULL' ENTERED AT 14:18:31 ON 07 SEP 2006 L10

FILE 'HCAPLUS, USPATFULL' ENTERED AT 14:18:43 ON 07 SEP 2006 5 DUP REMOV L9 L10 (0 DUPLICATES REMOVED)

FILE HOME

L11

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 SEP 2006 HIGHEST RN 905963-91-9 6 SEP 2006 HIGHEST RN 905963-91-9 DICTIONARY FILE UPDATES:

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

## FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Sep 2006 VOL 145 ISS 11

THIS PAGE LEFT BLANK

FILE LAST UPDATED: 6 Sep 2006 (20060906/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE USPATFULL FILE COVERS 1971 TO PATENT PUBLICATION DATE: 7 Sep 2006 (20060907/PD) FILE LAST UPDATED: 7 Sep 2006 (20060907/ED) HIGHEST GRANTED PATENT NUMBER: US7103915 HIGHEST APPLICATION PUBLICATION NUMBER: US2006200885 CA INDEXING IS CURRENT THROUGH 5 Sep 2006 (20060905/UPCA) ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 7 Sep 2006 (20060907/PD) REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2006 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2006

=> log hold
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE

0.00 -1.50

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:27:40 ON 07 SEP 2006